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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,942	07/21/2003	Marco Pappagallo	05986/100K504-US1	7691

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
10/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/624,942	PAPPAGALLO, MARCO	
	Examiner	Art Unit	
	JENNIFER MYONG M. KIM	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/30/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed on June 30, 2008 have been received and entered into the application.

Action Summary

The rejection of claims 1-9 and 11 under 35 U.S.C. 103(a) as being unpatentable over Geusens et al. (2001) of record is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 1-8, 10 and 11 under 35 U.S.C. 103(a) as being unpatentable over Urban et al. (2001) in view of Bader et al, both of record is being maintained for the reasons stated in the previous Office Action.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geusens et al. (2001) of record.

Geusens et al. teach that an 18-year-old boy presented with extreme back pain as the result of multiple vertebral fractures was treated with intermittent intravenous bisphosphonate such as **pamidronate**. (abstract). Geusens et al. teach that intermittent IV infusions of pamidronate were given at dose of 30mg infusion, 300 mg in total over 9 month. (page 390 right-hand column first sentence originated from left-hand column, bottom). The boy progressively recovered from **back pain** and is now, at age 20, fully ambulant. (abstract).

Geusens et al. do not teach the specific chronic spinal mechanical pain as being any back pain lasting more than twelve weeks which is not caused by cancer, or an osteoporotic compression fracture as defined in the specification page 7, and the treatment comprising providing prolonged pain relief.

However, it would have been obvious to one of ordinary skill in the art to employ pamidronate for the treatment of any back pain regardless of the cause because the effectiveness of pamidronate in pain management is well taught by Geusens et al. One would have been motivated to employ pamidronate for the treatment of any pain regardless of its cause in order to achieve the beneficial analgesic effect of pamidronate in the patient disclosed by Geusens et al. who progressively recovered from suffering from an extreme back pain with the treatment comprising pamidronate. There is a reasonable expectation of successfully treating any pain particularly back pain regardless of a cause because pamidronate treatment in the patient disclosed by Genuses recovered from the back pain with administration of pamidronate, therefore, the analgesic effect of pamidronate would be retained and it would be effective of

treating pain regardless of the etiology of how the patient conceived pain. With regard to the limitation of providing prolonged pain relief set forth in claim 1, such is obvious because Geusens et al. teach that intermittent IV infusions of pamidronate were given at dose of 30mg infusion, 300 mg in total over 9 month. Genusens et al's duration of therapy over 9 month comprising administration of pamidronate obviously provided "prolonged" pain relief because the boy progressively recovered from **back pain over 9 month therapy** and is now, fully ambulant.

Claims 1-8, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urban et al. (2001) in view of Bader et al, both of record.

Urban et al. teach that the bisphosphonate, zoledronate (30mcg/kg, s.c.) produced a significant anti-allodynic effect in rats. (abstract).

Urban et al. do not teach the intravenous administration of zoledronic acid for the treatment of pain.

Bader et al. report that bisphosphonates and their salts including zoledronate has been used as parenteral preparations for intravenous infusion and injection and preferably made available and utilized. (column 1, lines 14-26).

It would have been obvious to one of ordinary skill in the art to employ zoledronic acid for the treatment of pain in intravenous administration because zoledronic acids is well-known to be administered intravenously and preferably made available and utilized in parenteral infusion and injection formulations as taught by Bader et al. One would have been motivate do employ zoledronic acid in preferred parenteral preparations

including intravenous injection in order to provide alternative parenteral preparations next to subcutaneous injectable taught by Urban. There would have been a reasonable expectation of successfully administering zoledronic acid intravenously for the treatment of pain because intravenous infusion and injection formulation of zoledronate are preferably made available to be utilized as reported by Bader et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicant's arguments filed June 3, 2008 have been fully considered but they are not persuasive. Applicant argues that the amended claims recite that the bisphosphonate provides "prolonged pain relief" and the specification defined prolonged pain relief to mean "relief from chronic mechanical pain for a duration of more than one month, preferably for 3 month, and more preferably for 6 month". This feature rebuts the *prima facie* obviousness rejection because it is unexpected. This is not found to be persuasive because Geusens teach that pamidronate was given at a dose of 30mg infusion, 300mg in total over 9 month. Therefore, it would have been obvious to one of

ordinary skill in the art that the pamidronate provided prolonged pain relief in total over 9 month because the pamidronate therapy was continued during those 9 month time and because pamidronate is taught to be effective for the treatment of pain as taught by Geusens. Applicant argues that the specification discloses data supporting unexpected result that intravenously administered 1.2mg/kg of pamidronate once a day for three days reported no pain at 2, 4 and 6 months post -pamidronate therapy. This is not found persuasive because the teaching of Geusens of continual administration pamidronate having analgesic activity for 9 months encompasses the instantly claimed limitations of providing prolonged pain relief. Applicant argues that Urban, subcutaneous zoledronate produced an anti-allodynic effect in rats. However, allodynia is a condition in which ordinary non-painful stimuli evoke pain. This is not found to be persuasive because Urban at the title teach the antinociceptive effects of zoledronate for the treatment of pain and suggest that zoledronate has therapeutic potential for use in hyperalgesia (the excessive sensitiveness or sensibility to pain). (see title, and abstract). Therefore, Urban's suggestion for the employment of zoledronate for the treatment of any pain is clear by this teaching. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1617

Jmk
October 3, 2008